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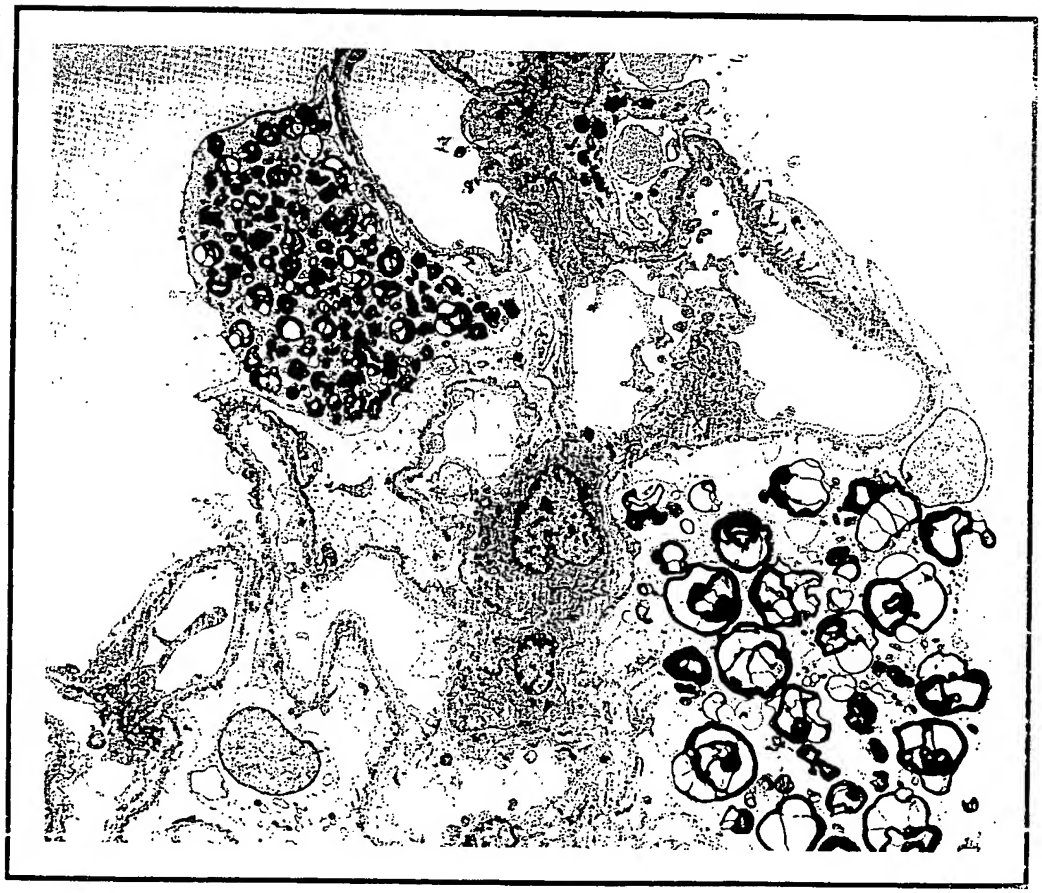

The Official Journal of the
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Cover Legend:

Fig 2. Electron micrograph of glomerular capillary loops in a patient with Fabry's disease. Lamellar and myelinoid inclusions are accumulated in visceral epithelial cell cytoplasm. (Original magnification ×1,500.) See Fukushima et al, p. 952.

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NATIONAL KIDNEY FOUNDATION POSITION PAPER

Bicarbonate Dialysate for Continuous Renal Replacement Therapy in Intensive Care Unit Patients With Acute Renal Failure

Martine Leblanc, MD, Luz Moreno, MD, Orlandus P. Robinson, CHT, Mihaly Tapolyai, MD, and Emil P. Paganini, MD

● Lactate-buffered peritoneal solution traditionally has been used as dialysate for continuous renal replacement therapy (CRRT) in the United States because no bicarbonate solution is commercially available. Since 1994, the Cleveland Clinic Foundation Dialysis Unit has prepared a bicarbonate solution (sodium 144 ± 3 mEq/L, HCO_3 37 ± 2 mEq/L, potassium 3 or 4 mEq/L, calcium 3.0 ± 0.3 mEq/L, and magnesium 1.4 ± 0.3 mg/dL) replicating the dialysate for chronic intermittent hemodialysis. No solute precipitation, as calcium or magnesium salts, were observed, and several cultures of the solution, performed at various time periods, remained negative. Fifty critically ill acute renal failure patients have been treated with bicarbonate-CRRT. All patients were in multiple organ failure and required mechanical ventilation; 37 were receiving vasopressors. Forty-four continuous venovenous hemodialysis sessions and eight continuous arteriovenous hemodialysis sessions were performed with a mean duration of 7.8 ± 6.1 days. The mean inflow dialysate rate was 1,249 ± 225 mL/hr and the mean outflow rate (dialysate plus ultrafiltration) was 1,399 ± 237 mL/hr; the inflow rate was constantly kept lower or equal to the outflow rate to avoid an enhanced potential for backfiltration. No related fever spikes or sepsis episodes were noted. The metabolic control achieved during bicarbonate-CRRT was good, with the following mean (±SD) daily values: blood urea nitrogen 70.3 ± 29.0 mg/dL, creatinine 3.6 ± 1.3 mg/dL, sodium 135.7 ± 3.7 mEq/L, potassium 4.6 ± 0.5 mEq/L, chloride 99.9 ± 4.6 mEq/L, carbon dioxide content 21.4 ± 3.4 mEq/L, calculated anion gap 14.4 ± 4.8 mEq/L, arterial pH 7.39 ± 0.05, arterial PCO_2 36.6 ± 5.4 mm Hg, total calcium 8.7 ± 0.9 mg/dL (corrected for albumin 9.6), phosphorus 4.2 ± 1.4 mg/dL, and magnesium 2.06 ± 0.26 mg/dL. A subgroup of 13 patients was treated with two dialysate types, lactate-based solution (Dianeal 1.5%; Baxter Healthcare Corporation, Deerfield, IL) for 3.2 ± 1.5 days and bicarbonate solution for 7.4 ± 1.6 days, and the obtained metabolic control under both types of dialysate was compared. Mean values ± SD (with probability values) obtained with lactate dialysate versus bicarbonate dialysate were as follows: blood urea nitrogen 77.6 ± 34.4 mg/dL versus 71.0 ± 20.8 mg/dL (P = NS), creatinine 4.1 ± 0.9 mg/dL versus 3.3 ± 1.6 mg/dL (P = NS), sodium 132.8 ± 4.8 mEq/L versus 135.6 ± 2.9 mEq/L (P = 0.04), chloride 95.8 ± 5.4 mEq/L versus 98.5 ± 4.2 mEq/L (P = NS), carbon dioxide content 17.8 ± 3.1 mEq/L versus 21.8 ± 3.4 mEq/L (P = 0.002), calculated anion gap 19.3 ± 4.4 mEq/L versus 15.2 ± 3.8 mEq/L (P = 0.008), arterial pH 7.36 ± 0.07 versus 7.40 ± 0.06 (P = NS), arterial PCO_2 32.1 ± 5.3 mm Hg versus 37.8 ± 3.8 mm Hg (P = 0.01), total calcium 8.3 ± 1.1 mg/dL versus 8.8 ± 1.0 mg/dL (P = NS), phosphorus 4.7 ± 1.3 mg/dL versus 3.8 ± 1.4 mg/dL (P = NS), magnesium 1.95 ± 0.14 mg/dL versus 2.04 ± 0.34 mg/dL (P = NS), and glucose 200.5 ± 80.4 mg/dL versus 146.7 ± 40.4 mg/dL (P = 0.04). The bicarbonate solution is simple to prepare and is cost-effective. In our experience, its use as dialysate for CRRT is safe, free of complications, and provides an excellent metabolic control.

INDEX WORDS: Continuous renal replacement therapy; bicarbonate dialysate; lactate-based dialysate; acid-base status; acute renal failure.

ONE OF THE major aims of renal replacement therapy in patients with chronic or acute renal failure (ARF), besides the control of azotemia and electrolyte disturbances, is the correction of the associated metabolic acidosis. It is known that metabolic acidosis can lead to several detrimental effects: an increase in protein turnover with consequent muscle protein degradation and enhanced catabolism,[1-3] progression of bone lesions through dissolution of mineral buffers,[4] and a depression of myocardial contractility consequent to a lower response to circulating catecholamines.[5,6]

It is now well accepted that acetate dialysis, particularly high-efficiency acetate dialysis, can lead to vascular instability and hypoxia.[7] In critically ill patients, bicarbonate hemodialysis has been associated with less intradialytic hypotension than acetate hemodialysis.[8] Despite a hemodynamic advantage, some technical problems relating to on-line bicarbonate dialysate preparation still remain: bicarbonate instability with the potential for calcium and magnesium salt precipitation over time and the risk of bacteremia and

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endotoxemia consequent to a more rapid bacterial growth in the liquid bicarbonate concentrate.[9,10]

Continuous renal replacement therapies (CRRTs) are well recognized as advantageous alternatives to intermittent hemodialysis for intensive care unit (ICU) ARF patients. To our knowledge, at the present time, most centers in the United States performing CRRT are using lactate-buffered peritoneal solutions as dialysate and also, in certain cases, as replacement fluid. Sterile bicarbonate solution is available for replacement fluid for continuous hemofiltration, but, since it is very expensive, it is generally not used for dialysate for other forms of CRRT.

In the past, there has been concern that the infusion of large amounts of D,L-lactate from Ringer's solution or peritoneal dialysis solution could lead to increased catabolism and cerebral dysfunction.[9,11] To date, only one study has been published on the use of bicarbonate-based dialysate for CRRT. It included five pediatric patients treated by continuous arteriovenous hemodialysis (CAVHD), and the results suggested an improvement of the metabolic acidosis with bicarbonate dialysate compared with lactate or acetate dialysates.[12]

Since 1994, the Cleveland Clinic Foundation Dialysis Unit has prepared a bicarbonate-based solution as an alternative to the usual lactate-buffered solution used as dialysate for CRRT. This new solution is now considered the standard dialysate for ICU ARF patients treated by CRRT at this institution. Our present objective is to report the preparation procedure of the bicarbonate dialysate and the favorable experience with its use in a group of 50 ICU patients.

MATERIALS AND METHODS

Patients

Since 1994, the prepared bicarbonate solution has been used as dialysate for 50 ICU ARF patients treated by CRRT. The following patient data were recorded: demographics; Acute Physiology Age Chronic Health Evaluation (APACHE II) score at the time of admission to the ICU; hemodynamic parameters at initiation of CRRT; ventilatory, pressor, and nutritional support during CRRT; type and duration of CRRT; inflow dialysate rate and outflow (dialysate plus ultrafiltration) rate; and blood flow rate when on continuous venovenous hemodialysis (CVVHD). Daily metabolic parameters (from routine early morning laboratory examinations), including blood urea nitrogen (BUN), creatinine, sodium, potassium, chloride, carbon dioxide content (bicarbonate and dissolved carbon dioxide), calculated anion gap, arterial pH, arterial PCO_2, total calcium, albumin, phosphorus, magnesium, glucose, and arterial lactic acid, when available, obtained during the entire period of CRRT with the bicarbonate dialysate, were recorded.

A subgroup of 13 patients treated by CRRT with lactate dialysate, generally followed by bicarbonate dialysate, served as its own control to compare the metabolic control achieved. The data from this subgroup were analyzed separately. Daily metabolic parameters and duration of CRRT under each type of dialysate were recorded.

Blood was obtained from indwelling arterial catheters. Serum chemistries were analyzed by usual laboratory methods (Beckman Synchron CX-3, Brea, CA); blood gases were processed by an automated blood gas analyzer (model 288; Ciba-Corning, Medfield, MA). Samples for arterial blood L-lactate were collected and stored on ice and were analyzed using an enzymatic method (model 2300; WSI, Antioch, OH).

Dialysate Solution Preparation

The solution was prepared by the dialysis technicians using volumetric single-pass dialysis machines (Althin-1000; Althin CD Medical Inc, Miami, FL). These single-patient proportioning dialysis machines use two concentrates (acid and bicarbonate), and mix heated water (treated by reverse osmosis in our dialysis unit) with the dialysate concentrate to create a solution with the correct ionic composition and physiologic temperature. The conductivity was set to correspond to a sodium concentration of 140 mEq/L and the chosen temperature was 37°C. The obtained dialysate was then inflowed at 500 to 900 mL/min into the dialysate compartment of a high-flux, hollow-fiber, polysulfone membrane dialyzer (F-80; Fresenius AG, Bad Homburg, Germany) and allowed to transfer by backfiltration into the dialyzer blood compartment, from which it was drained into sterile 12- to 15-L plastic bags (Cycler Drainage Set; Baxter Healthcare Corporation, Deerfield, IL). The nondraining line of the dialyzer blood compartment was used for degassing and for solution sampling, while the unused dialysate port was clamped during the procedure. Figure 1 is a schematic representation of the procedure.

Filled plastic bags were sealed with plastic tie clamps after the procedure and kept at room temperature for a maximum of 72 hours. If not used within 72 hours, they were discarded. One hemofilter was used to prepare approximately 12 to 15 bags, each containing 12 to 15 L of dialysate solution. Two bags were hung on a large circular pole for use during CRRT. The solution so produced was a replication of the standard dialysate used during intermittent bicarbonate hemodialysis, and thus no further justification for its use was judged necessary.

Solute Concentrations in Dialysate

Several aliquots of dialysate solution were sent for laboratory analysis. The mean solute concentrations obtained are shown in Table 1; those of the traditional lactate solution (Dianeal 1.5%, Baxter Healthcare Corporation) are also indicated for comparison.

Although the preparation procedure of the dialysate solution was sterile, the solution itself cannot be considered as a

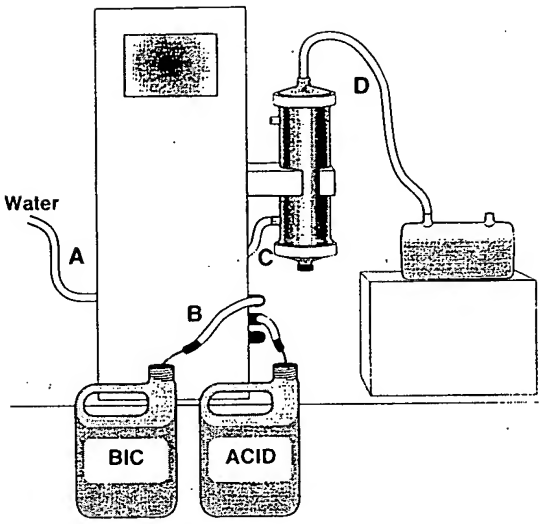

Fig 1. Schematic representation of the preparation of the bicarbonate solution used as dialysate. Reverse osmosis-treated water (A) was mixed by proportioning dialysis machines with acid and bicarbonate concentrates (B). The dialysate so produced was then inflowed into the dialysate compartment (C) and allowed to transfer by backfiltration into the dialyzer blood compartment, from which it was drained into sterile plastic bags (D).

sterile fluid. However, several cultures of dialysate samples taken every day for a period of 3 weeks did not show any microbial growth. Since the presence of endotoxins is possible,[10] this solution has not been used as replacement fluid, but only as dialysate. No solute precipitation (as calcium or magnesium salts) was observed within the time of use and in several bags observed over more than 2 weeks, but the presence of microprecipitation cannot be excluded.

Techniques for Continuous Renal Replacement Therapy

Either continuous arteriovenous or venovenous hemodialysis sessions (44 CVVHD and eight CAVHD) were performed in this study. The hemofilters used in 46 sessions were hollow-fiber, polyacrylonitrile-membrane PAN-50 (Asahi, Asahi Medical Co LTD, Tokyo, Japan); in the six remaining sessions, hollow-fiber polysulfone-membrane F-4 (Fresenius AG) filters were used. For CVVHD, a blood pump (Baxter Healthcare Corporation) maintained the blood flow rate between 150 and 200 mL/min. Most sessions were performed without any anticoagulation; heparin in doses between 250 to 750 U/hr was administered in only 12 cases. The dialysate was infused into the appropriate dialysate compartment of the filter at the prescribed rate via volumetric infusion pumps (McGaw Accu Pro; American Edwards Laboratories, Irvine, CA); similar pumps also controlled the outflow (dialysate plus ultrafiltration) rate at the prescribed level, as previously described.[13] The inflow rate was always kept either lower or equal to the outflow rate to avoid a positive pressure favoring backfiltration.[14,15] While backfiltration and backdiffusion can still occur when large-pore membrane filters are used, the bicarbonate solution is similarly used as dialysate in chronic dialysis patients and has not been associated with deleterious clinical effects.

Statistics

Results are presented as mean values ± SD. Data were analyzed with Student's paired *t*-test, and $P < 0.05$ was considered significant.

RESULTS

The 50 cases treated with the bicarbonate dialysate were critically ill patients from surgical and medical ICUs and presented ARF requiring dialytic support. Only two cases had a primary diagnosis of severe liver failure, and all were in multiple organ failure at initiation of CRRT. There were 33 men and 17 women with a mean age of 59.9 ± 16.6 years old and a mean APACHE II score at ICU admission of 19.6 ± 5.4. At initiation of CRRT, 76% of patients were oligoanuric and mean hemodynamic parameters showed the following values: mean arterial blood pressure 78 ± 22 mm Hg, heart rate 101 ± 14 beats/min, and cardiac output and systemic vascular resistances (available for only 43 patients) 7.4 ± 3.9 L/min and 758 ± 427 dyne · sec · cm^5, respectively. During CRRT, all patients were mechanically ventilated and 37 were receiving vaso-

Table 1. Composition of the Bicarbonate Solution and Dianeal 1.5%

	Dianeal 1.5%	Bicarbonate Solution
Sodium (mEq/L)	132	144 ± 3
Potassium (mEq/L)	3-4*	3.7 ± 0.2
Calcium (mEq/L)	3.5	3.0 ± 0.3
Magnesium (mEq/L)	1.5	1.4 ± 0.3
Chloride (mEq/L)	102	111 ± 3
Lactate (mEq/L)	35	—
Bicarbonate (mEq/L)	—	37 ± 2
Acetate (mEq/L)	—	2-4†
Glucose (anhydrous, mg/dL)	1300	205 ± 15

NOTE. Solute concentrations in the bicarbonate dialysate are the mean values ± SD of seven aliquots sampled from different bags after preparation of the solution.

* Potassium, as potassium chloride, was added to obtain a concentration of 3 or 4 mEq/L.

† Acetate was not measured, but was assumed to reach a concentration of 2 to 4 mEq/L, as reported for bicarbonate dialysate in chronic hemodialysis.

Table 2. Metabolic Control of the 50 Patients During Continuous Renal-Replacement Therapy Using the Bicarbonate Dialysate

BUN (mg/dL)	70.3 ± 29.0
Creatinine (mg/dL)	3.6 ± 1.3
Sodium (mEq/L)	135.7 ± 3.7
Potassium (mEq/L)	4.6 ± 0.5
Chloride (mEq/L)	99.9 ± 4.6
Carbon dioxide (HCO_3 + dissolved carbon dioxide; mEq/L)	21.4 ± 3.4
Calculated anion gap (mEq/L)	14.4 ± 4.8
Arterial pH	7.39 ± 0.05
Arterial PCO_2 (mm Hg)	36.6 ± 5.4
Total calcium (mg/dL)	8.7 ± 0.9
Albumin (g/L)	2.9 ± 0.7
Phosphorus (mg/dL)	4.2 ± 1.4
Magnesium (mg/dL)	2.06 ± 0.26
Glucose (mg/dL)	163.0 ± 73.6

NOTE. The results are expressed as mean values ± SD of the daily parameters obtained during the entire period of CRRT with the bicarbonate dialysate.

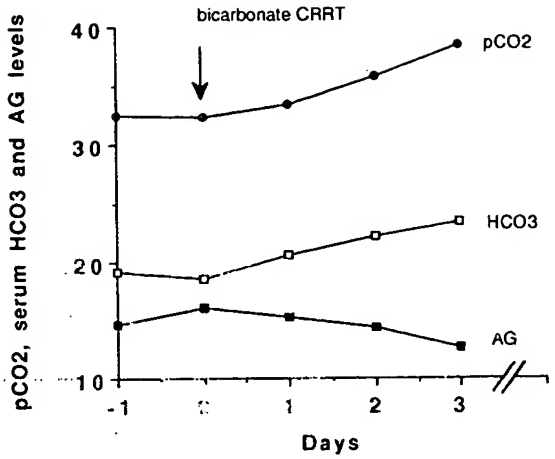

Fig 2. Mean daily arterial PCO_2, serum bicarbonate concentration (HCO_3), and calculated anion gap (AG) before and during bicarbonate-CRRT for the 50 patients. Results after the broken horizontal axis were obtained the day preceding the end of CRRT. The units of measure are mm Hg for PCO_2 and mEq/L for HCO_3 and anion gap.

pressors for hemodynamic instability; 20 patients were receiving total parenteral nutrition, 14 patients were being tube fed, and 16 patients were receiving no nutritional support. The mean arterial lactic acid level within 24 hours before CRRT initiation, available for only 22 patients, was 7.1 ± 5.2 mEq/L; subsequent monitoring of lactic acid concentrations was too erratic to draw any firm conclusion.

Forty-four CVVHD and eight CAVHD sessions using the bicarbonate solution as dialysate were performed over a mean of 7.8 ± 6.1 days (range, 2 to 24 days). Two patients initially treated by CAVHD were changed over time to CVVHD for practical purposes. The mean inflow dialysate rate was 1,249 ± 225 mL/hr and the mean outflow (dialysate plus ultrafiltration) rate was 1,399 ± 237 mL/hr, leading to a mean hourly ultrafiltration rate of 148 ± 78 mL. The metabolic control achieved for the 50 cases during bicarbonate-CRRT, expressed as the means of daily measurements, is shown in Table 2. Figure 2 presents the mean daily results of acid base status of the 50 patients prior to initiation, during the first days of treatment, and before discontinuation of CRRT.

A subgroup of 13 patients was treated with lactate-based dialysate (Dianeal 1.5%) for a mean period of 3.2 ± 1.5 days and with bicarbonate dialysate for a mean period of 7.4 ± 1.6 days, and the metabolic control achieved under both types of dialysate was compared. As shown in Table 3, the acid base balance was slightly improved during bicarbonate-CRRT, with a sig-

Table 3. Comparison of the Metabolic Control With Lactate Dialysate and Bicarbonate Dialysate for the 13-Patient Subgroup

	Dianeal 1.5%	Bicarbonate Solution	Probability Value
BUN (mg/dL)	77.6 ± 34.4	71.0 ± 20.8	NS
Creatinine (mg/dL)	4.1 ± 0.9	3.3 ± 1.6	NS
Sodium (mEq/L)	132.8 ± 4.8	135.6 ± 2.9	0.04
Chloride (mEq/L)	95.8 ± 5.4	98.5 ± 4.2	NS
Carbon dioxide (HCO_3 + dissolved carbon dioxide; mEq/L)	17.8 ± 3.1	21.8 ± 3.4	0.002
Calculated anion gap (mEq/L)	19.3 ± 4.4	15.2 ± 3.8	0.008
Arterial pH	7.36 ± 0.07	7.40 ± 0.06	NS
Arterial PCO_2 (mm Hg)	32.1 ± 5.3	37.8 ± 3.8	0.01
Total calcium (mg/dL)	8.3 ± 1.1	8.8 ± 1.0	NS
Phosphorus (mg/dL)	4.7 ± 1.3	3.8 ± 1.4	NS
Magnesium (mg/dL)	1.95 ± 0.14	2.04 ± 0.34	NS
Glucose (mg/dL)	200.5 ± 80.4	146.7 ± 40.4	0.04

NOTE. The results are expressed as mean values ± SD of daily values obtained during CRRT, with either lactate dialysate or bicarbonate dialysate.

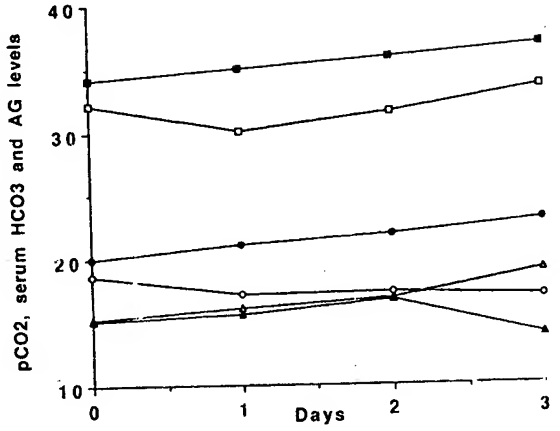

Fig 3. Mean daily arterial PCO_2, serum bicarbonate concentration (HCO_3), and calculated anion gap (AG) at initiation and during 3 days of CRRT with each type of dialysate (lactate and bicarbonate) for the 13-patient subgroup. The units of measure are mm Hg for PCO_2 and mEq/L for HCO_3 and anion gap. (■) PCO_2 with bicarbonate; (□) PCO_2 with lactate; (●) HCO_3 with bicarbonate; (○) HCO_3 with lactate; (▲) AG with bicarbonate; (△) AG with lactate.

nificant increase in blood carbon dioxide (from 17.8 to 21.8 mEq/L) and a decrease in the calculated anion gap (from 19.3 to 15.2 mEq/L). In addition, with comparable arterial pH levels, the arterial PCO_2 was higher during bicarbonate-CRRT, suggesting less ventilatory requirement to achieve the same arterial pH. Mean values for BUN, creatinine, and phosphorus were not different, while total calcium and magnesium were maintained within normal limits using both types of dialysate. Sodium and glucose were significantly closer to normal with the bicarbonate dialysate. Figure 3 shows the evolution of the acid base status during the first 3 days with each type of dialysate in the 13-patient subgroup.

No complications resulting from the use of the bicarbonate-based dialysate were observed. No spike in temperature following therapy initiation, no related sepsis, and no evidence of solute precipitation before use or at bedside were noted. Hypothermic episodes occurred in several cases and were attributed in part to the extracorporeal circuit; rewarming procedures, such as blankets, heating lamp, or dialysate warming, were only occasionally used. Sixteen patients (32%) were discharged alive from the ICU. The other 34 patients died after a mean of 30.2 ± 24.1 days of hospitalization, leading to a mortality rate of 68%. Of the 16 survivors, 11 required intermittent hemodialysis, at least temporarily, while the other five were free of any dialytic support at discharge from the ICU. The 37 patients treated exclusively with bicarbonate-CRRT and the 13 patients treated with lactate and bicarbonate dialysates had similar mortality rates (61.5% *v* 64.9%; P = NS).

A cost evaluation revealed that a 12- to 15-L bag of the bicarbonate solution costs $13.68, including all the material and the technicians' working time. Thus, the price of the bicarbonate dialysate is between $0.91 and $1.14 per liter. The cost of a 5-L bag of Dianeal 1.5% ranges between $10 and $20 dollars, a price of $2 to $4 per liter.

DISCUSSION

During CRRT, there is a bicarbonate loss consequent to diffusive and convective fluxes that must be replaced. It has been estimated that, assuming a relatively stable blood level, a patient could loose nearly 750 mEq of bicarbonate per day with CAVHD.[16] The loss of bicarbonate is expected to be even greater when high ultrafiltration rates are reached. When lactate dialysate is used, the lost bicarbonate is in part regenerated from the absorbed lactate, which, when metabolized, consumes an equivalent number of hydrogen ions and restores the alkali reserve.[17] If the endogenous capacity to metabolize lactate is altered, as in liver failure, this bicarbonate loss could potentially lead to an important decrease in serum bicarbonate level. On the other hand, critically ill patients frequently present high lactic acid levels, usually from overproduction due to poor peripheral perfusion, with an associated metabolic acidosis. While sodium bicarbonate is frequently given to improve the acid base balance of these patients, it has not been demonstrated to change their morbidity or mortality rates.[18-20]

However, one pertinent question that arises is the potential detrimental effect of a significant net administration of lactate anions through CRRT to patients who already may have high lactic acid levels and an altered endogenous metabolizing capacity. In our 22 patients for whom lactic acid was monitored within 24 hours of CRRT initiation, the mean lactic acid level was over 7 mEq/L; thus, many of these patients presented with hyperlactatemia, defined by a level

higher than 5 mEq/L.[18] Dalal et al have shown in chronic hemodialysis patients that although L-lactate high-efficiency hemodialysis was hemodynamically well tolerated, it was associated with hypoxemia and a delayed correction of pH and plasma HCO_3 concentrations.[21] Davenport et al investigated the effect of an exogenous lactate load in patients with chronic renal failure, ARF, and both acute liver plus renal failure treated by intermittent hemofiltration.[22] All patients developed hyperlactatemia, which was more severe in the liver failure cases. In addition, during treatment, serum lactate levels increased from 1.0 to 4.3 mEq/L, while bicarbonate increased only from 19.3 to 21.3 mEq/L in patients with ARF. The increase in bicarbonate was smaller for ARF cases than for chronic renal failure cases, suggesting that ARF may be accompanied by a relative intolerance to lactate anions.

In an effort to control the acid base status of ARF patients treated by CRRT with a more physiological buffer, and concerned about the possible detrimental effects of a lactate load given during these CRRT when using lactate-based dialysate, we prepared a bicarbonate solution that was a replication of the dialysate used for chronic intermittent hemodialysis. The procedure is both simple and cost-effective. Although expected at the prevalent concentrations,[23] no precipitation of calcium or magnesium salts has been observed; furthermore, as the calcium and magnesium blood concentrations were well maintained during bicarbonate-CRRT, it can be assumed that no significant changes in the composition of the solution occurred within the time of use since the diffusive balance was not affected. In addition, since the source water has not been generated as "sterile," the resultant dialysate should be considered "clean" but not sterile. While the dialysate has been passed through a filtration process and is devoid of bacterial activity, as demonstrated by the absence of colony counts on cultures, the possible presence of endotoxin has not been eliminated.[15,24] Because this possibility exists, we cannot recommend the use of this solution for anything other than dialysate, as it also applies for CRRT. In our series, no septic episodes related to CRRT have been recorded, with the precaution of maintaining the inflow rate lower than the outflow rate to reduce the risk of backfiltration.[14,15]

Good metabolic control was achieved in the 50 patients treated by bicarbonate-CRRT, with electrolytes, calcium, and magnesium levels and the acid base balance maintained within normal or near normal limits. The comparison of the metabolic parameters for the subgroup of 13 patients treated with lactate and bicarbonate dialysates suggests that the bicarbonate solution may be associated with an improved acid base status and better-maintained sodium and glucose concentrations. One could argue that the improved acid base status obtained under bicarbonate dialysate may be consequent to changes in ventilator parameters, partial recovery of endogenous renal acidifying capacity over time, weight loss with reduced bicarbonate volume of distribution, longer treatment period with bicarbonate than with lactate dialysate, or even the sequence of solutions used for treatment, as the bicarbonate dialysate generally followed the lactate dialysate. A prospective study will be required to completely address these issues. However, among these 13 patients, eight died while they were still on CRRT without any evidence of renal function recovery, and four of the five survivors required intermittent hemodialysis after CRRT cessation, thus indicating no significant improvement in endogenous acidifying capacity. Despite similar arterial pH under both types of dialysate, the arterial PCO_2 was significantly higher, but normal, under bicarbonate dialysate, as opposed to relatively low with the lactate solution. This most probably indicates a reduced need for respiratory compensation to maintain a normal pH. The elevated PCO_2 content of bicarbonate solution (when over 35 mEq/L) could have induced an increase in blood PCO_2, or the greater transfer of bicarbonate from the dialysate solution to blood could have caused a metabolic alkalosis resulting in a hypocapnia and an associated hypoxemia, as described in continuous hemodialysis patients.[25,26] However, despite an improved correction of the metabolic acidosis, overall there was no evidence of metabolic alkalosis in our patients, and since all were mechanically ventilated, the PCO_2 and PO_2 were more a reflection of the ventilator parameter adjustments. Although we cannot demonstrate a difference in lactic acid levels under both types of dialysate, since they were monitored erratically and only in a minority of patients, the lower calculated anion gap while

treated with the bicarbonate dialysate compared with the lactate dialysate suggests an underlying decrease in lactate levels with the bicarbonate solution. A decrease in anion gap was found to correlate with the decrease in lactate level in the only previous study using bicarbonate dialysate in five pediatric patients treated with CAVHD.[12] Finally, the observed similar levels of BUN, creatinine, and phosphorus confirm that patients received a comparable dialysis dose delivery.

The difference in plasma sodium is explained by the higher tonicity of the bicarbonate dialysate compared with the relatively hypotonic lactate solution; the lower blood glucose can result from the more physiological glucose concentration in the bicarbonate solution, although other carbohydrate sources or insulin administration were not systematically considered. A net positive transfer of glucose from the dialysate to the patient has been demonstrated during CAVHD with Dianeal 0.5% and shown to increase in a linear mode with the dialysate flow rate.[27] The glucose load is expected to be even greater with Dianeal 1.5%, which has a nonphysiological glucose concentration of 1,300 mg/dL.

The survival rate of the 50 patients was 32%, confirming that the outcome of ARF occurring with multiple organ failure remains poor. As already reported, ARF cases treated by CRRT are frequently more complicated and unstable than those treated by intermittent modalities, explaining in part the high mortality rates observed.[28,29] The mortality rates were similar among patients treated exclusively with bicarbonate dialysate compared with those treated with both types of dialysate. However, this study was not designed to establish any firm conclusion regarding differences in hemodynamic profile or in outcome in relation to the bicarbonate solution. Further evaluation regarding morbidity/mortality outcome will be needed.

In conclusion, the bicarbonate solution prepared as described is relatively simple, is safe, and may be cost-effective in centers performing many CRRTs. Its use, exclusively as dialysate during CRRT, is free of complications and is associated with a well-maintained metabolic control. The more physiologic bicarbonate-buffered dialysate seems to result in an improved acid base balance. In ARF patients presenting with severe metabolic acidosis and in cases of lactate intolerance, such as liver failure, it appears theoretically advantageous to use this solution as dialysate for CRRT.

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